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Development and evaluation of a retroperitoneal dialysis porcine model

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Key words
end-stage kidney disease – renal insufficiency – peritoneal dialysis – hemodialysis – retroperitoneum – peritoneal diffusion

Abstract. Objectives: We attempted to create a surgical model to evaluate the retroperitoneal space for the ability to transfer solutes through the retroperitoneal membrane. Our dual objectives were to develop a technique to assess the feasibility of retroperitoneal dialysis (RPD) in a porcine model. Methods: We incorporated two 35-kg Yorkshire pigs for this pilot study. In the first animal, we clamped renal vessels laparoscopically. In the second animal, we embolized renal arteries. In both animals, we dilated the retroperitoneal space bilaterally and deployed dialysis catheters. We measured serum creatinine (Cr), urea, and electrolytes at baseline 6 hours before the dialysis and every 4 hours after. Results: We successfully created retroperitoneal spaces bilaterally and deployed dialysis catheters in both animals. In the first animal, dialysate and plasma Cr ratio (D/P) on the left and right side were 0.43 and 0.3, respectively. Cr clearance by 40 minutes of dialysis treatment was 6.3 mL/min. The ratio of dialysate glucose at 4 hours dwell time to dialysate glucose at 0 dwell time (D/D_0) for left/rights sides were 0.02 and 0.02, respectively. kt/V_{urea} was 0.43. In the second animal, D/P Cr for left/right sides were 0.34 and 0.33, respectively. kt/V_{urea} was 0.17. We euthanized the pigs due to fluid collection in the peritoneal space and rapid increase of serum Cr, urea, and electrolytes. Conclusions: We demonstrated the feasibility of creation of a functionally anephric porcine model with successful development of retroperitoneal spaces using balloon inflation. Notwithstanding minimal clearance and limited diffusion capacity in this experiment, additional studies are needed to examine potential use of retroperitoneal space for peritoneal dialysis.

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Introduction

Dialysis removes waste and excess water from the blood in patients with end-stage kidney failure [1, 2]. The two well-recognized clinically viable forms of dialysis include peritoneal dialysis (PD) and hemodialysis (HD). PD involves the infusion of glucose and solute solution into a patient's peritoneal cavity, at which time the peritoneal membrane allows the exchange of solutes between the blood stream and the dialysis fluid filling the peritoneal cavity, thus facilitating removal of waste products from the blood. Unfortunately, despite meticulous preventive strategies, PD is often associated with complications, such as spontaneous bacterial peritonitis, which may lead to membrane sclerosis and subsequently a significant decrease in filtration capacity. Additionally, PD catheters often become obstructed with omentum or visceral contents leading to failure of proper dialysis [3]. Those patients who are on hemodialysis often fail conventionally used veins for vascular access and new advanced transhepatic and trunslumbar inferior vena cava techniques [4, 5]. When all options are exhausted, patients are in urgent need for alternative options for dialysis, and this represents a great challenge for the treating physician [3, 6, 7].

To our knowledge, the retroperitoneal space has not previously been evaluated for dialysis. We hypothesized that this new form of dialysis would provide both an adequate transfer of solutes through the retroperitoneal membrane and would likely result in fewer complications due to the procedure occurring outside of the peritoneal cavity. Thus, we initiated a preliminary effort to establish an experimental access technique and to assess the feasibility of retroperitoneal dialysis (RPD) in a porcine model.

Methods

We obtained an Institutional Animal Care and Use Committee (IACUC) approval to

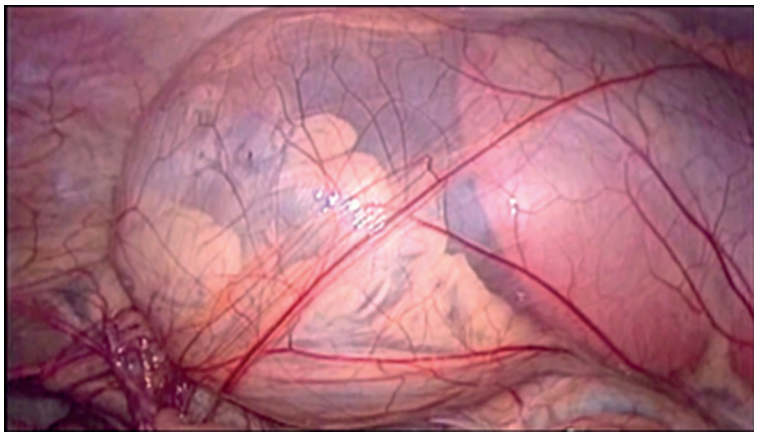

Figure 1. Dilation of retroperitoneal space under direct transperitoneal laparoscopic vision.

perform this experiment. We used two 35-kg female Yorkshire pigs for this study. Upon arrival, the animals were acclimatized for 2 days preoperatively. Surgery was performed in a dedicated surgery suite meeting the requirements of the Guide for the Care and Use of Laboratory Animals for survival surgery.

Presurgical preparation

We performed proper anesthesia according to IACUC protocols. A preanesthetic mixture of xylazine (2 mg/kg), ketamine (20 mg/kg), and atropine sulfate (0.04 mg/kg) was injected intramuscularly prior to the procedure. Ceftiofur sodium (3.0 – 5.0 mg/kg) was also administered intramuscularly. We intubated the trachea for subsequent mechanical ventilation and gas anesthesia delivery, and cannulated the ear vein for intravenous fluid therapy. We continuously monitored vital signs, body temperature, and muscle tone throughout the procedure to assess the level of anesthesia. Mechanical ventilation was performed throughout the procedure under continuous delivery of 1.5 – 2.5% isoflurane anesthesia and tidal volumes ranging from 300 to 400 mL.

Creation of retroperitoneal space and dialysis catheter deployment

After general anesthesia was induced, we placed the animal in a supine position. We prepared the abdomen and flank with povidone-iodine scrub and drape. Prior to induction of general anesthesia, a blood sample was collected for baseline plasma creatinine (Cr), blood urea nitrogen (BUN), and glucose levels.

We then created the retroperitoneal space and deployed the dialysis catheter under direct laparoscopic vision. We made bilateral 1-cm flank incisions in the paraspinal line below the costal margin. Using a Kelly clamp, we dilated a tract to the retroperitoneal space bilaterally and deployed the dilating balloon (AutoSuture PDB 1000, Covidien, Mansfield, MA, USA) and inflated the balloon on each side under direct laparoscopic vision with 800 cc of air (Figure 1). The balloons were removed, and we deployed the dialysis catheters using the tunneling method as previously described for peritoneal space catheter placement [8]. We fixed the dialysis catheter to the subcutaneous tissue after creating a 2-cm subcutaneous tunnel by another Dacron clamp. We used adult-size CF-5560 Flex-Neck ExxTended Peritoneal Catheter (Merit Medical Systems, Inc., South Jordan, UT, USA) and VP-211 PAC Dialysis Catheter Implantation System (Merit Medical Systems, Inc.). Once it was placed, we sutured the dialysis catheters in place with 2-0 prolene on the flank, to prevent accidental removal, followed by a protective vest.

After placement of retroperitoneal dialysis catheters on both sides, we confirmed each catheter's proper placement and functionality by instilling 1 L of dialysate fluid on each side. We removed all fluid immediately with no dwell time. This step completed the installation procedure, and then we proceeded with renal artery clamping.

Surgical technique for renal artery occlusion and vein clamping (Pig 1)

In our first animal, we used the traditional laparoscopic approach to dissect and clip the renal arteries and veins. A pneumoperitoneum was created using a Veress needle, and a total of three trocars were placed. One 12-mm trocar was placed at the umbilicus for the camera, and two 12-mm operative trocars were pkaced on each side. Under direct visualization, we mobilized the renal hilum using a bipolar grasper and harmonic scalpel. Once the renal artery and vein were located,

a small incision on the peritoneum was made in order to mobilize the vessels. Once we circumferentially dissected the vessels, we clipped both artery and vein using laparoscopic hem-o-lok clips (Teleflex Medical, Research Triangle Park, NC, USA). Once we completely devascularized both kidneys, we used laparoscopic ultrasound to confirm that each kidney had complete interruption of blood supply.

Surgical technique for renal artery embolization (Pig 2)

After the first procedure, we modified our technique of renal artery clamping in order to avoid any disruption of the peritoneum and to maintain the integrity of the retroperitoneal space, which had been disrupted in our first experiment. The second pig was placed in the supine position on a radiolucent table. We prepped the bilateral groins and draped in a standard, sterile fashion. Using ultrasonography, we identified the right common femoral artery and punctured using a 21-gauge micropuncture access needle, followed by the access wire and 4-Fr introducer sheath. We introduced and placed a 0.035-in Bentson wire (Cook Medical, Bloomington, IN, USA) into the distal aorta, and a sheath exchange was performed to place a larger 5-Fr sheath. Once the sheath was in place, an Omni-Flush catheter (Angiodynamics, Latham, NY, USA) was inserted over the Bentson wire to approximately the T12-L1 position. We performed an aortogram with 20 cc of 50% concentrated contrast in order to identify the bilateral renal arteries. We then exchanged the Omni-Flush for a Cobra catheter (Cook Medical) followed by removal of the Bentson wire and insertion of an 0.035-in Angled Glidewire (Boston Scientific, Natick, MA, USA). We initially cannulated the left renal artery. Once the catheter was advanced into position at the origin of the renal artery, we embolized the artery using MWCE-35-4/3-Tornado coils (x4) and MWCE-35-6/3 Tornado coils (x2). We then performed an arteriogram to confirm complete occlusion of the renal artery. Following the occlusion of the left renal artery, our attention was then placed on the right renal artery. We reintroduced the Angled glidewire through the Cobra catheter and cannulated the right renal artery. Once we achieved access to the right renal artery, we placed the catheter at its origin and embolized the right renal artery using MWCE-35-6/3 Tornado coils (x4).

After we embolized the bilateral renal arteries, we performed a completion angiogram using the Omni-Flush catheter confirming that the renal arteries were completely occluded and there was no delayed filling of the kidneys. We then removed the wire, catheter, and sheath. Because of the percutaneous approach with a small sheath, a pressure dressing over the puncture site was satisfactory for hemostasis. No heparin was given during the case. The animals were extubated, transported, and housed in individual cages. We monitored the animal continuously during the recovery time. Postoperative pain was properly controlled according to the protocol with Buprinex (buprenorphine hydrochloride; 0.005 – 0.02 mg/kg) every 8 hours.

We monitored the serum plasma Cr, urea, and electrolyte panel postoperatively every 6 hours for the first 36 hours post-procedure. We initiated the RPD once the pigs' plasma Cr level reached 5 mg/dL.

Retroperitoneal dialysis

In order to test the diffusion process, we infused 1 liter of a 4.25% glucose peritoneal dialysate solution (4.25 g/L per 100 mL, hyperosmolar and hypertonic solution) in each side. We used commercially-available, sterile, nonpyrogenic dialysate solution (DIANEAL PD-2 solution from Baxter, Deerfield, IL, USA). We measured the inflow and outflow times, and a dwell time of 40 minutes was allowed after the infusion. The inflow time was recorded from the time when the dialysate bag was connected to the peritoneal dialysis catheter until the entire 1L dialysate liquid was in retroperitoneal space. The outflow was timed from the time that the peritoneal dialysis catheter was connected to the drain bag until the maximum amount of dialysate fluid was drained. Connection and disconnection of the retroperitoneal catheter to the dialysate fluid bag was all performed aseptically. We measured and recorded the

Table 1. Retroperitoneal dialysis: intraoperative data.

	Pig 1			Pig 2	
	Dialysis 1	Dialysis 2	Dialysis 3	Dialysis 1	Dialysis 2
Volume (mL) of dialysate introduced into RP space (left)	1,000	1,000	1,000	1,000	1,000
Volume (mL) of dialysate introduced into RP space (right)	1,000	1,000	1,000	1,000	1,000
Time (min/sec) to introduce dialysate into RP space (left)	4:47	3:47	3:05	3:35	3:50
Time (min/sec) to introduce dialysate into RP space (right)	3:04	2:53	3:04	4:05	3:50
Total time (min) to introduce dialysate into RP space	7:51	6:40	6:09	7:40	7:40
Volume (mL) of dialysate drained (left)	280	320	519	275	320
Volume (mL) of dialysate drained (right)	240	216	170	220	240
Total volume (mL) dialysate drained	520	536	689	495	560
Time (min/sec) to drain dialysate from RP space (left)	5:08	6:29	12:14	7:00	8:50
Time (min/sec) to drain dialysate from RP space (right)	3:35	8:49	11:50	6:30	9:30
Total time (min/sec) to drain dialysate from RP space	8:43	15:18	14:50	13:30	18:20

RP = retroperitoneal.

amount of fluid drained from each side after each treatment.

We measured the plasma Cr, urea, and glucose levels after the above instillation and outflow of dialysis solution was complete. In addition, dialysate samples were also collected upon drainage of the dialysate solution from the retroperitoneal cavity to measure dialysate osmolality, creatinine, urea, and glucose levels.

We assessed the blood and dialysate collections for solute concentration dialysate/plasma ratios (Cd/Cp). Cd/Cp is concentration differences of a solute between the two sides of the retroperitoneal membrane, and we measured this for urea and Cr 40 minutes after infusion of the dialysate upon drainage of retroperitoneal fluid. For glucose in the dialysate, absorbance rate is expressed as Cd/Cd_0 where Cd_0 is initial glucose concentration at time zero. Cd/Cp is not applicable for glucose since the glucose absorbed systemically is rapidly metabolized.

For creatinine clearance, the following formula was applied:

CreCl = creatinine clearance (mL/min) = CdVd/Cpt

Cp = creatinine concentration (mg/dL) in plasma; Cd = creatinine concentration (mg/dL) in dialysis fluid; t = time in minutes required to complete the exchange; and Vd = volume of dialysis fluid (mL) returned at the end of the exchange

To calculate adequacy of clearance of urea, which is calculated as a weekly value, the equation kt/V_{urea} was used, whereby:

$K_{urea} = (D_{urea}/P_{urea}) \times$ dialysate volume (L) = volume cleared in L/day

t = number of days (usually calculated per 1 week = 7 days)

V_{urea} = volume of distribution of urea = total body water = ~ 0.7 × body wt of pig

Results

We successfully created the retroperitoneal space bilaterally in both animals. The mean operative time for creation of the retroperitoneal spaces and placement of dialysis catheters was 65 minutes on the left side and 95 minutes (including vessel embolization) on the right side. The average blood loss was 50 mL on both sides, and there were no intraoperative complications during the procedures.

For pig 1, baseline plasma Cr, BUN, and glucose were 1.0 mg/dL, 10 mg/dL, and 17 mg/dL, respectively. Plasma Cr immediately after surgery, 6 hours, 12, 18 and 24 hours was 1.9 mg/dL, 2.2 mg/dL, 3.7 mg/dL, 4.9 mg/dL,

Table 2. Plasma Cr, urea, and glucose levels during the experiment for Pig 1.

	Urea (mg/dL)	Creatinine (mg/dL)	Sodium (MEQ/L)	Potassium (MEQ/L)	Chloride (MEQ/L)	CO_2 (MEQ/L)	Glucose (mg/dL)
Baseline	10	1.0	140	6.4	104	26	17
Immediately post clamp	10	1.9	142	6.5	104	27	16
6 hours post clamp	14	2.2	143	4.1	110	14	48
12 hours post clamp	25	3.7	140	6.7	110	22	89
18 hours post clamp	37	4.9	142	5.5	111	21	60
Dialysis began	44	5.8	138	5.3	102	23	94
4 hours post dialysis	44	5.9	132	4.9	98	23	131
8 hours post dialysis	46	6.2	131	5.5	98	23	75
12 hours post dialysis	45	6.3	134	4.3	99	22	109
18 hours post dialysis	60	8.8	125	5.6	88	24	85
20 hours post dialysis	60	9.1	126	5.7	89	24	112
Animal euthanized							

Table 3. Plasma Cr, urea, and glucose levels during the experiment for Pig 2.

	Urea (mg/dL)	Creatinine (mg/dL)	Sodium (MEQ/L)	Potassium (MEQ/L)	Chloride (MEQ/L)	CO_2 (MEQ/L)	Glucose (mg/dL)
Baseline	4.0	1.3	143	4.5	100	34	101
Immediately post op	7	1.9	142	4.6	103	28	22
6 hours post clamp	23	3.1	144	3.0	121	17	101
12 hours post clamp	36	4.5	143	3.5	115	20	81
18 hours post clamp	26	3.4	144	2.2	125	13	37
24 hours post clamp	43	6.6	143	4.0	113	20	63
Dialysis began	50	8.3	139	3.8	107	19	82
4 hours post dialysis	33	4.8	145	2.8	124	13	44
8 hours post dialysis	81	13.8	139	8.1	90	31	93
10 hours post dialysis	83	13.7	140	6.7	90	29	265
18 hours post dialysis	78	13.6	147	5.9	9.8	26	74
Animal euthanized							

and 5.8 mg/dL. For pig 2, baseline plasma Cr, BUN, and glucose were 1.3 mg/dL, 7 mg/dL, and 101 mg/dL, respectively. Plasma Cr immediately after surgery, 12, 18, 24, and 30 hours were 1.9 mg/dL, 3.1 mg/dL, 4.5 mg/dL, 3.4 mg/dL, and 6.6 mg/dL, respectively.

RPD was initiated when plasma Cr levels reached 5 mg/dL. Cr reached this level after being in an anephric state for 24 hours and 30 hours in pig 1 and pig 2, respectively. RPD was performed every 8 hours with a bilateral refill of 1 L dialysate fluid. More details of the RPD intraoperative data are demonstrated in Table 1. The mean infusion time was 4.5 minutes (range 3 – 7 minutes). After a dwell time of 40 minutes, the dialysate fluid was drained. For pig 1, a total of 3 RPD treatments were performed. The left side drained 280 mL (28%), 320 mL (18%), and 519 mL (37%) after the first, second, and third treatments, respectively. On the right side, 240 mL (24%), 216 mL (12%), and 170 (11%) mL of fluid were drained after each respective treatment. The total fluid drained after the first treatment was 520 mL (26%). Larger total volumes were drained after the second and third treatments (536 mL (15%) and 689 mL (14%), respectively). Time to drain the dialysate fluid ranged from 5 to 15 minutes (Table 1). Two RPD treatments were performed for pig 2. In this pig, the left side drained 275 mL (27.5%) and 320 (18.5%) mL of fluid after the first and second treatments, respectively. The right side drained 220 mL (22%) and 240 mL (13.5%). Total drain output in pig 2 was 495 mL (49.5%) and 560 mL (15.5%) after first and second treatments, respectively. Similar values for drain times were observed in pig 2, ranging from 6 to 18 minutes (Table 1).

Plasma creatinine, urea, and glucose levels at baseline and follow-up evaluations for pig 1 and 2 are demonstrated in Tables 2 and Table 3, respectively. For pigs 1 and

Table 4. Plasma creatinine clearance, urea, and glucose calculations on pigs 1 and 2.

Variables	Pig 1	Pig 2
Creatinine	L-side D/P creatinine = 2.7/6.3 = 0.43. R-side D/P creatinine = 1.9/6.3 = 0.3. Average dialysate Cr = average (2.7 and 1.9) = 2.3 mg/dL. Cr clearance by 40 min dialysis treatment = (Cd × Vd)/(Cp × t) = (2.3 f 689 mL)/(6.3 × 40 min) = 6.3 mL/min.	Based on 3rd RPD exchange in pig 1, let us presume 3 treatments per day with removal of 0.689 L at the end of each treatment. K_{urea} = volume of urea cleared per day = (D_{urea}/P_{urea}) × dialysate volume (L) = (33/45) × (0.689 × 3) = 1.52 L. Volume of distribution of urea = total body water = 0.7 × body weight of pig = 0.7 × 35 = 24.5 kg. Therefore kt/V_{urea} = (1.52 L × 7 days)/24.5 kg = 0.43.
Glucose	L-side D/D_0 glucose = 66/4250 = 0.02. R-side D/D_0 glucose = 76/4250 = 0.02.	L-side D/D_0 glucose = > 600/4,250 = unable to calculate as dialysate glucose was above detection limit. R-side D/D_0 glucose = > 600/4,250 = unable to calculate as dialysate glucose was above detection limit. Note: D/D_0 glucose could not be calculated due to detection limit of lab.
Urea	Based on 3rd RPD exchange in pig 1, let us presume 3 treatments per day with removal of 0.689 L at the end of each treatment. K_{urea} = volume of urea cleared per day = (D_{urea}/P_{urea}) × dialysate volume (L) = (33/45) × (0.689 × 3)= 1.52 L. Volume of distribution of urea = total body water = 0.7 × body weight of pig = 0.7 × 35 = 24.5 kg. Therefore, kt/V_{urea} = (1.52 L × 7 days)/24.5 kg = 0.43.	Based on 2nd RPD exchange in pig 2, let us presume 3 treatments per day with removal of 0.560 L at the end of each treatment. K_{urea} = volume of urea cleared per day = (D_{urea}/P_{urea}) × dialysate volume (L) = (30/83) × (0.560 × 3) = 0.604 L. Volume of distribution of urea = total body water = 0.7 × body weight of pig = 0.7 × 35 = 24.5 kg. Therefore kt/V_{urea} = (0.604 L × 7 days)/24.5 kg = 0.17.

2, clearance and adequacy calculations were done using the dialysate and blood values measured during the 3rd RPD treatment (10/5/2013 at 22:00) and the 2nd RPD treatment (5/12/2014), respectively (Table 4).

Termination of the study

The first pig was euthanized due to increasing fluid accumulation in the peritoneal space. The second pig was euthanized due to a rapid increase of plasma Cr, BUN, and electrolyte levels.

Necropsy results

At the time of the necropsy, a total of 3.5 L of fluid was drained from the peritoneal space of pig 1. There was no evidence of abdominal injuries or bleeding. We believe that the intraperitoneal fluid accumulation was due to peritoneal rupture during renal hilum and vasculature exposure at the beginning of the procedure. This fluid accumulation in the peritoneal space was the main reason that the animal was euthanized. Necropsy for the pig 2 demonstrated a significant fluid accumulation in the retroperitoneal space. There was no evidence of bleeding or injuries to the peritoneum or other surrounding structures.

Discussion

PD is a method of renal replacement therapy in which the peritoneal membrane serves as a barrier across which clearance of urea and other small solutes occurs [2, 9, 10]. However, PD patients may run into complications that necessitate temporary or permanent cessation of PD therapy. Peritonitis is the most common cause of morbidity and mortality in patients with peritoneal dialysis [11]. Other complications include inadequate solute removal and volume overload, and the rarer entity encapsulating peritoneal sclerosis [12, 13, 14]. The use of different treatment modalities becomes necessary in the setting of PD cessation. HD is the only alternate dialysis therapy currently

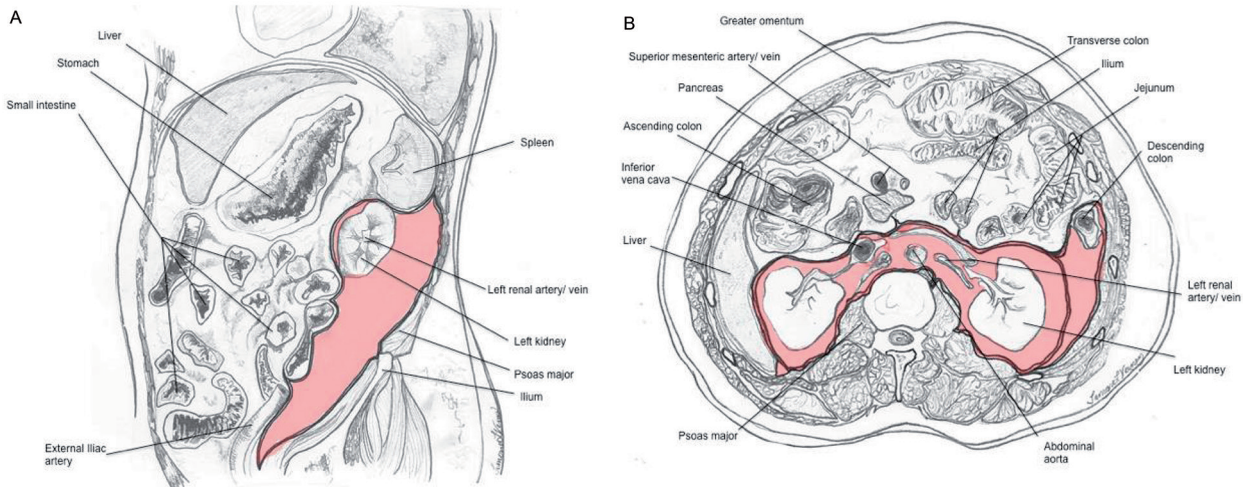

Figure 2. Delineation of retroperitoneal space in humans.

available. However, studies have shown that patients new to HD have a higher relative risk of death in the first several months of treatment, and HD is significantly more costly when compared to PD [15]. For these reasons, we explored the feasibility of using the retroperitoneal space for toxin exchange as an alternative to peritoneal dialysis.

In this pilot study, we describe a novel technique for dialysis through the retroperitoneal space in a swine model. The goals were two-fold. Firstly, we wanted to develop an experimental technique to create functionally-anephric animals by devascularizing the porcine kidneys while maintaining the integrity of the retroperitoneal space. Secondly, we wished to assess this space for its capacity for fluid and solute exchange. To our knowledge, this technique for dialysis has not been previously evaluated. Complete interruption of blood supply to the kidneys, through either clamping or embolization, as well as the creation of a retroperitoneal space on both sides on each pig was successfully achieved. Although the current pilot data showed that there was no diffusion and no effective clearance of toxins, whether ultimately RPD is feasible warrants additional studies.

The data was initially promising from pig 1, but this was likely deceptive due to leakage of dialysate into the peritoneal cavity. In order to clamp the renal vessels on pig 1, traditional laparoscopic peritoneal approach was used. The limitation of this technique was that the peritoneum was dissected in order to approach the renal vessels and a window was created that allowed the fluid to migrate from the retroperitoneal into the peritoneal space. In this pig, the blood analysis showed stable numbers for plasma urea, creatinine, sodium, potassium, chloride, and carbon dioxide at the 26-, 30-, 34-, and 36-hour mark after baseline measurements in response to the start of treatment. Even in the short dwell time of 40 minutes, serum Cr levels demonstrated that there was a minimal Cr clearance from the blood into the dialysate, with D/P Cr values of 0.43 for the left side and 0.3 for the right side. In humans on PD, the 4-hour D/P creatinine value ranges from 0.34 to 1.03. Initially it was interpreted as promising data indicating that small toxins can be effectively removed. However, later it was identified that a leakage of dialysate into the peritoneal space most likely caused these data values. Similarly, there was a rapid shift of glucose into the blood, indicated by a significant drop in dialysate glucose compared to the initial concentration of 4.25 g/L. This indicates adequate blood supply (capillary networks) within the retroperitoneal space thus allowing for solute diffusion. Again, the drop in glucose was likely due to diffusion via the peritoneal (rather than retroperitoneal) membrane. A caveat that needs to be considered is that if there were inflammatory cells in the retroperitoneal space, due to recent surgery and creation of retroperitoneal cavities, these cells can metabolize the glucose and thus also cause lowering of dialysate glucose. In terms of urea, which is one of the most important toxins to be removed in humans on peritoneal dialysis, the target weekly kt/V value is 1.7, which signi-

fies adequate toxin removal. This is usually achieved via 4 daily treatments with dwell times of at least 1.5 hours. Our calculations based on the 3rd treatment in pig 1 project a weekly value of 0.43, which was encouraging since this is based on only 3 daily treatments that are 40 minutes each. We conclude that toxin removal in pig 1 likely occurred across the peritoneal rather than the retroperitoneal membrane.

In pig 2 we were able to successfully devascularize the porcine kidneys using novel embolization techniques keeping the peritoneal membrane intact. Pig 2 initially showed a decrease in plasma Cr, urea, potassium, carbon dioxide, and glucose after dialysis had begun. However, at later timepoints, there was a rapid increase in plasma urea, creatinine sodium, potassium, carbon dioxide, and glucose. There are several possible mechanisms for this decrease and increase. Even though some diffusion occurred in the retroperitoneal space, these results suggested possibly less than adequate toxin removal, which may be due to insufficient membrane surface area and/or blood supply or due to technique limitation in our preliminary experiments. Finally, the ultrafiltration component of the dialysis, which is defined as the ratio of infused and drained dialysate fluid, on both pigs was not successful in these two preliminary models. Typically, it is expected that more fluid is drained after a dwell time, given that the dialysate is effectively pulling fluid from the systemic blood circulation. Fluid accumulation in the retroperitoneal space in pig 2 may have been due to dialysis catheter malfunction, which precluded effective drainage of the fluid.

Conclusions

We developed a technique for successful creation of isolated retroperitoneal spaces using balloon inflation, with concurrent renal artery embolization to induce a functionally anephric state. Although retroperitoneal dialysis in these preliminary models appeared ineffective given suboptimal uremic toxin removal, these experiments suggest that retroperitoneal space can be created for dialysis and that additional studies and models are needed to further explore the feasibility and dialysis parameters including clearance and ultrafiltration.

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